Kantonsspital St.Gallen

Resistance Development in Escherichia coli at different pH following Delafloxacin and Ciprofloxacin Challenge

Baharak Babouee Flury

Delafloxacin , a novel dual-targeting non-zwitterionic fluoroquinolone, has received approval by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) and Community-acquired Bacterial Pneumonia (CPA) in adults, caused by designated susceptible bacteria. Delafloxacin (DLX) has excellent activity against Gram-positive organisms and anaerobes and similar MICs to those of ciprofloxacin against Gram-negative bacteria . DLX has anionic character at neutral pH (~7-7.4) and is mainly found in uncharged form at slightly acidic pH, which differs from other fluoroquinolones (eg, ciprofloxacin, levofloxacin, moxifloxacin), that are present as cation at acidic pH and mainly zwitterions at higher values, and for which activities decrease (higher MICs) in acidic environments . This feature may explain the highly improved potency of DLX in acidic environments, as the non-ionized form is considered as more diffusible through biological membranes . In contrast to CIP, DLX shows similar affinity to both enzymes, topoisomerase IV and DNA gyrase, in both Gram-positive and Gram-negative bacteria (6). In addition, inhibition of the efflux system potentiates the activity of DLX against E. coli in colony biofilms and pathogenic E. coli strains in stationary-phase cultures .

Standard in vitro antibiotic susceptibility testing conditions do not always reflect micro-environmental conditions of the infection site. The pH of purulent abscess fluids range from 5.5 to 7.2 . Same applies for biofilms- including those of E. coli- where pH ranges between 3.5 to 6.0 have been documented . Having the importance of the micro-environment of the infection site in mind, we sought to determine resistance evolution of E.coli against DLX and CIP in acidic and neutral environment.

type of project	fundamental research
status	ongoing - follow up
start of project	2021
end of project	2022
project manager	Baharak Babouee Flury